MINUTES

Executive Recombinant DNA Committee
Eleventh Meeting

May 25, 1978 9:00 a.m.
Building 31 Room 7A24

Present: Dr. DeWitt Stetten, Chairman
Dr. Bernard Talbot, Executive Secretary
Dr. W. Emmett Barkley
Dr. Mary Fink
Dr. Joe Held
Mr. Joe Hernandez for Dr. Joseph Perpich
Dr. Leon Jacobs
Dr. Daphne Kamely
Dr. Ruth Kirschstein
Dr. John Nutter
Mr. Richard Riseberg
Dr. Wallace Rowe
Mrs. Helen Schroeder for Dr. William Raub
Dr. Maxine Singer
Dr. Rudolf Wanner

Absent: Dr. William Gartland
Dr. Malcolm Martin
Dr. Joseph Perpich
Dr. William Raub
Dr. John Seal

Guests: Dr. Fred Bergmann
Mr. Steven Bernard
Dr. Arthur Heming
Dr. Jerry Roberts
Mr. James Schriver

The Executive Recombinant DNA Committee (ERDC) had been sent in advance of the meeting: (1) "The Schriver Report" (i.e., April 14 memorandum from Mr. Schriver to Dr. Stetten, "Research Involving Recombinant DNA Molecules--Dr. Charles A. Thomas, Jr., Harvard University"); (2) "The Bloch Committee Report" (i.e., "Report of the Ad Hoc Committee on Recombinant DNA at Harvard Medical School," April 18, 1978); (3) Comments on the "Schriver Report" prepared by Charles A. Thomas, Jr., May 3, 1978; (4) "Comments on the Bloch Committee Report" prepared by C. A. Thomas, Jr., May 5, 1978; and (5) A May 12 letter from Dean Daniel Tosteson of the Harvard Medical School to Dr. Stetten.

MAJOR CONCLUSIONS

The ERDC members discussed this case and came to the following major conclusions:

1. All of the documents, including the Schriver Report and the Bloch Committee Report, are in substantive agreement as to the major facts.

2. All the information available to the ERDC indicates that at no time were Dr. Thomas' laboratory practices out of compliance with applicable guidelines or conducted in a manner that would constitute a hazard.

3. There was a failure to comply with an NIH directive requiring that a Memorandum of Understanding and Agreement (MUA) be filed with NIH by November 15, 1976. The responsibility for the fact that this requirement was not satisfied until over a year later rests jointly with Dr. Thomas, Harvard University, and the NIH.

SPECIFIC DISCUSSION

1. Recombinant DNA Research in Dr. Thomas' Laboratory Prior to July 7, 1976: Prior to the publication of the NIH Guidelines for Research Involving Recombinant DNA in the Federal Register on July 7, 1976, investigators were voluntarily following the "Asilomar guidelines." All evidence available to the ERDC indicates that Dr. Thomas conducted recombinant DNA experiments in his laboratory prior to July 7, 1976, in conformity with the Asilomar guidelines.

2. Use of the Term "P3" in Dr. Thomas' April 9, 1976, Letter to Dr. Stetten: The Schriver Report discusses an April 9, 1976, letter from Dr. Thomas to Dr. Stetten in which the term "P3 facility" is used. The ERDC noted that the term "P3" was not used in the "Asilomar guidelines" which were then applicable and with which Dr. Thomas' experiments were in conformity. The definition of P3 was evolving during this period. The provisional definition of P3 as approved by the Recombinant DNA Molecule Program Advisory Committee and published in the "Proposed Guidelines" of January 1976 was significantly modified by NIH during the spring of 1976, as reflected in the Guidelines published by NIH on July 7, 1976. Therefore, confusion during the spring of 1976 as to precisely what P3 meant is understandable. Even today when the NIH definition of P3 is clearly stated in the NIH Guidelines, individual universities, including Harvard, have added additional requirements which must be met before they give certification as "P3."

3. Mention of Recombinant DNA in Dr. Thomas' Grant Applications: The Schriver Report points out that, in Dr. Thomas' original grant applications and in continuation applications, specific mention of the use of recombinant DNA techniques was not made. The ERDC, however, noted that grants are given by NIH to meritorious investigators to pursue the scientific questions described in their grant applications; it is permissible and in fact desirable that they

use the latest tools and techniques to pursue these goals. Dr. Thomas' original grant application was made during 1974, before recombinant DNA became a widely used research technique. The continuation applications submitted by Dr. Thomas were brief, but this is not rare; indeed investigators frequently submit brief continuation applications. Those submitted by Dr. Thomas did cite publications from his laboratory in which recombinant DNA techniques had been used.

4. Recombinant DNA Research in Dr. Thomas' Laboratory Subsequent to July 7, 1976: All evidence available to the ERDC indicates that Dr. Thomas' laboratory practices subsequent to July 7, 1976, were in conformity with the NIH Guidelines. As noted in the Bloch Committee Report, there is "no evidence that work was conducted at any time in a manner that could constitute a hazard to the public or to individuals working in or near the laboratory."

Mr. Leslie Dach (whose December 6, 1977, Freedom of Information request led to the discovery that no MUA was on file with NIH for Dr. Thomas' recombinant DNA research) was provided copies of the Schriver Report and the Bloch Committee Report and asked to supply to the ERDC any further information he might have on this matter, including whether recombinant DNA research was ever performed in Dr. Thomas' laboratory out of compliance with applicable guidelines. Mr. Dach submitted no such information.

5. Failure to File an MUA with NIH by November 15, 1976: An August 26, 1976, memorandum from Dr. Fredrickson and Dr. Gartland to all NIH grantee institutions and contractors required that "a Memorandum of Understanding and Agreement (MUA) for each ongoing project involving recombinant DNA technology . . . be submitted to the NIH Office of Recombinant DNA Activities no later than November 15." On November 12, 1976, Dr. Thomas forwarded such an MUA to the Harvard Medical School (HMS) Recombinant DNA Committee for review and approval, and submission to NIH. Had that MUA been quickly approved and forwarded to NIH, there would have been no violation of NIH documentary requirements. However, since an MUA covering Dr. Thomas' recombinant DNA studies was, in fact, not forwarded by HMS to NIH until over a year later, there was a non-compliance. The history of the processing of this MUA by Harvard University is described in great detail in the Schriver Report and the Bloch Committee Report. Fault lies partly with Dr. Thomas (for example, he admits he "misspoke" to the HMS Recombinant DNA Committee in saying his grant renewal had been held up), partly with the HMS Recombinant DNA Committee (for example, they did not communicate the disposition of his MUA to Dr. Thomas in writing), and partly with NIH (for example, Dr. Thomas' grant was renewed by NIH in January 1977, without an MUA although there was information on file at NIH indicating that Dr. Thomas had been doing recombinant DNA research in the past and that an MUA had been requested).

6. Continuation of Recombinant DNA Research by Dr. Thomas After November 15, 1976: The August 26, 1976, memorandum from Dr. Gartland says that an MUA must be submitted to NIH by November 15, 1976, "for each ongoing project involving recombinant DNA technology." It does not specifically state whether the lack of submission of an MUA means that a project must not continue

beyond November 15, 1976. The Schriver Report interprets the August 26, 1976, memorandum as requiring cessation on November 15, 1976, of any project for which an MUA was not on file with NIH. The Bloch Committee Report notes "there was disagreement about whether ongoing P2 work could continue while the MUA was being reviewed."

One member of the ERDC felt that the issuance of revised instructions about MUAs by NIH in October 1977, and the reaction of scientists to these revised instructions, attest to the lack of clarity of the August 26, 1976, memorandum. The October 1977 memorandum specifically introduces the concept of a "proposed MUA" as sent to NIH by the institution and an "MUA approved by the Office of Recombinant DNA Activities" which is now required before NIH gives "authorization for use of funds to conduct recombinant DNA experiments."

7. Revised Procedures Since November 1976: The ERDC noted that procedures have already been revised both at Harvard and at NIH which should greatly decrease the likelihood of such a case occurring again.

As noted in the Bloch Committee Report, "Harvard University committees now issue an explicit statement when the MUA is received, that no recombinant DNA work can be performed until the MUA has been approved. . . . The HMS Recombinant DNA Committee now reports in writing to the investigator all of its relevant conclusions and votes."

New NIH procedures have been instituted (they were already in effect prior to December 1977, when the lack of an MUA on file at NIH covering Dr. Thomas' research was discovered) which include: (1) the requirement that all research grant applications to NIH include on the first page of the application the statement "this application does/does not involve recombinant DNA," and (2) the requirement for prior approval of MUAs by NIH, as discussed above.

In addition, the proposed revision of the NIH Guidelines which is now being prepared contains more explicit language discussing the roles and responsibilities of the principal investigator, the institution, its institutional biosafety committee, and the NIH.

8. Responsibility for Non-compliance: As discussed above, the ERDC concluded that responsibility for this non-compliance lies partly with Dr. Thomas, partly with Harvard University, and partly with NIH. The ERDC agreed with the Bloch Committee Report that "there were ambiguities in the rules and procedures at the time in both Federal and University circles."

RECOMMENDATIONS

For over 5 months, Dr. Thomas has not been allowed to use NIH funds for recombinant DNA research. He has suffered because of this proscription and the accompanying publicity. The December 14, 1977, letter prohibiting NIH funds to be used for recombinant DNA research on Grant GM 21740 said that NIH was "withholding approval . . . pending clarification of prior compliance by this investigator /Dr. Thomas/ with the NIH Guidelines."

Because the Executive Recombinant DNA Committee found that Dr. Thomas' laboratory practices were conducted in compliance with the NIH Guidelines, and that there has been only a non-compliance with documentary process for which responsibility must be shared by NIH and Harvard University, as well as by Dr. Thomas, the ERDC voted unanimously to recommend to the Director, NIH, that Dr. Thomas be permitted once again to use NIH funds for recombinant DNA research. It recommended that a letter be sent to Dr. Thomas, and that a similar letter be sent to Dean Tosteson at Harvard Medical School; suggested text was composed by one ERDC member at the meeting, read to the Committee, and endorsed in principle. It was refined by Committee members subsequent to the meeting. The ERDC recommended that the revision of the NIH Guidelines currently being prepared include a clear statement of the roles and responsibilities of NIH, institutions, institutional biosafety committees, and principal investigators, so that an incident of this sort does not occur again. The ERDC further voted unanimously that as an exception the minutes of this meeting be made available to the public.

cc:
Executive Recombinant DNA Committee Members
OD Staff
Dr. Bergmann
Mr. Bernard
Dr. Goldberg
Dr. Heming
Mr. Hernandez
Dr. Roberts
Mr. Schriver
Mrs. Schroeder